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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/502,424	Applicant(s) KILIAN ET AL.	
	Examiner Malgorzata A. Walicka	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-107* is/are pending in the application.

4a) Of the above claim(s) *7-10,16-26,30,33,35-60,62-64,68-70,80 and 102-107* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,11-15,27-29,32,34,61,65-67,71-79,101 and 312* is/are rejected.

7)☒ Claim(s) *1-15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

The examiner acknowledges the Preliminary Amendment filed on February 11, 2000. Claims 65 to 107 have been entered as requested. The lengthy amendment to the specification has not been entered. A substitute specification is required pursuant to 37 CFR 1.125(a) because preliminary amendment to the specification filed on February 11, 2000, which comprises five pages, was not entered due to its length. As indicated in the restriction requirement, paper No. 9, a substitute specification is required.

The Response to the Restriction Requirement, filed on Oct.12, 2001, paper No. 12, is acknowledged. Applicants elected, with traverse, claims 1-15, 27-40, 61, 65-93 and 100-107 of Group II, drawn to vertebrate telomerase gene, its variants and fragments. In response to the requirement of species election Applicants elected the variant described by SEQ ID NO:45.

Claims 1-107 are pending in the application. Claims 1-6, 11-15, 27-29, 31-32, 34, 61, 65-67, 71-79 and 101 readable on the elected species are the subject of this Office action; claims 7-10, 16-26, 30, 33, 35-60, 62-64, 68-70, 80-100 and 102–107 are withdrawn from consideration as directed to the nonelected invention.

Detailed Office Action

1. Restriction/Election

In Response to the Restriction Requirement, filed on Oct.12, 2001, paper No. 12, Applicants elected, with traverse, Group I claims 1-15, 27-40, 61, 65-93 and 100-107.

The Applicants traverse the restriction requirement as it applies to Group I-V. The traverse is on the ground that the examiner has restricted Groups I-IV whereas

these inventions are connected in their operation or effects with vertebrate telomerase. Applicants also argue that there is no undue burden on examiner to search the DNA sequences, the amino acid sequences and the antibody binding to the vertebrate telomerase. In addition, Applicants conclude that the examiner did not show that there is a burden of searching together for claims of Group I and IV and V which are directed to the process of using either telomerase cDNA or telomerase RNA.

The argument that Groups I-V are invention that are connected in their operation or effects with vertebrate telomerase is found nonpersuasive. The instant application is a US patent application to which the US restriction practice applies. Accordingly, DNA, expression vectors and host cells transformed with these vectors belong to one restriction group, the protein to the other. Also. antibodies and methods of use the protein or DNA are all in separate restriction groups.

Applicants are kindly reminded that restriction involves four factors: distinctness, independence, classification and burden to the examiner.

Protein and DNA encoding said protein (Group I and II) are distinct chemical entities and require different searching of patent and non-patent literature as revealed by their different classification. Though the searches are overlapping, they are not coextensive. Search of Group I would require search for host cell transformed with the expression vector, class 435, subclass 252.3 as well as class 536, subclass 23.2 encompassing DNA encoding enzymes. Search of these classes is unnecessary for the search of Group II that is classified in class 435 subclass 194. Thus, due to different classification, independence and different literature search restriction between Group I

and Group II is proper. Group III is classified in class 530, subclass 387.9 is drawn to antibody to the vertebrate and hybridoma cells for their production. Group IV drawn to a method of diagnosing cancer using the telomerase cDNA is classified in class 435, subclass 6. Inventions of Group I-IV are not only classified in distinct classes, but also are distinct or independent for reasons stated clearly in the restriction requirement, paper No. 8. However, to advance the prosecution the examiner withdraws the restriction between Groups IV and VI. Thus, the revised restriction requirement encompasses the following groups:

I. Claim 1-15, 27-40, 61, 65-93 and 100-107 drawn to DNA, expression vector and transformed host cell to produce recombinantly vertebrate telomerase, classified in class 435, subclass 252.3.

II. Claim 16-22, drawn to vertebrate telomerase, its variants and fragments, classified in class 435, subclass 194.

III. Claim 23-26, drawn to antibody and a hybridoma cell for their production, classified in class 530, subclass 387.9.

IV. Claim 41-49 and 94-99, drawn to a method of diagnosing cancer using telomerase cDNA, and a pattern of expression of telomerase RNA, classified in class 435, subclass 6.

V. Claim 50-53, drawn to transgenic animals where the telomerase gene is operably linked to a promotor effective for the expression of the gene, classified in class 800, subclass 13.

VI. Claim 54, drawn to a mouse having endogenous telomerase gene disrupted, classified in class 800, subclass 9.

VII. Claim 55-59, drawn to inhibitor of vertebrate telomerase, classified in class 435, subclass 184.

VIII. Claim 60, drawn to a method of treating cancer, comprising administering therapeutically effective amounts of telomerase inhibitor, classified in class 514,subclass 44.

IX. Claims 62-64 drawn to a method of identifying an effector of telomerase activity classified in class 536, subclass 184.

In conclusion, the Applicants' arguments have been found persuasive only as to rejoining of Group IV and V. The new restriction as written above is proper for reasons presented in the previous restriction requirement, paper No. 9, and is made FINAL.

In requirement of species election Applicant elected DNA described by SEQ ID NO:45. According to Applicants claims 1-15, 27-40, 61, 65-85, 91-93, 102, 104, 105 and 107 of Group I readable on the elected species. The examiner has found that, in addition, claims 66 and 101 are readable on the elected species, but claims 7-10, 30, 33, 35-40, 69-70, 80-90, 91, 93, 102, 104, 105 and 107 are not readable on DNA shown in SEQ ID NO:45. Thus, claims 1-3, 4, 5-6, 11-15, 27-29, 31-32, 34, 61, 65-67, 71-79 and 101 are examined in this Office action.

2. Objections

2.1. Specification

The specification does not comply with sequence rule because the sequence identification numbers are absent in many places. A substitute specification is required pursuant to 37 CFR 1.125(a) because preliminary amendment to the specification filed on February 11, 2000, which comprises five pages, was not entered due to its length.

A substitute specification filed under 37 CFR 1.125(a) must only contain subject matter from the original specification and any previously entered amendment under 37 CFR 1.121. If the substitute specification contains additional subject matter not of record, the substitute specification must be filed under 37 CFR 1.125(b) and must be accompanied by: 1) a statement that the substitute specification contains no new matter; and 2) a marked-up copy showing the amendments to be made via the substitute specification relative to the specification at the time the substitute specification is filed.

Sequence identification numbers should be added to Table 1 on page 22.

The usage of terms exon and intron is confusing in specification. The specification refers, on page 19, line 19 and further, to telomerase variants presented in Figure 7: "exons are deleted (see α, β, Fig. 7)." Also in the figure fragments Y, α and β are described as "exon(s) delated." On the other hand, fragments Y, 1, α, β, 2, 1, and X are called introns in the Sequence Listing (SEQ ID NO:18, 23, 25, 27, 29, 32).

On page 18, line 7 the word "an amplified" should be deleted. On page 56, line 2, Figure 1 should be Figure 2.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants' cooperation is requested in correcting any errors of which applicant may become aware.

2.2. Drawings

This application has been filed with informal drawings, see the attached notice of the draftsperson (PTO form 948), which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Figure 7 is illegible and confusing as to the usage of the terms exon and intron; see above. Position of fragment X is not marked in the figure.

Figure 10 A presents two sequences labeled as "*". The "*" sequence consisting of 36 bases is in the Sequence Listing (page 21) labeled as intron α, SEQ ID NO:25. Please use identifying and clear labels.

Figure 12 is illegible.

2.3. Claims

Claims 3-6, 61 and 65 refer to sequences presented in figures. The sequence rule 37 CFR § 1,821 paragraph (d) reads: "where the description or claims of a patent application discuss a sequence listing that is set forth in the "Sequence Listing" with paragraph (c) of this section, reference must be made to the sequence by the use of the assigned identifier (written as SEQ ID No:1, SEQ ID NO:2, SEQ ID NO:3, etc) in the text of the description or claims, even if the sequence is also embedded in the text of the

description or claims of the patent application. Therefore, as per rule cited above, claims 3-6, 61 and 65 should be amended to recite the SEQ ID NOS or additionally add SEQ ID NOs in parenthesis.

Claim 11 is objected to because of the following informalities: the word to is missing after according. Appropriate correction is required.

Claims **13-15** are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend form another multiply dependent claim; see MPEP § 608.01(n). Accordingly, the claims have **not been further treated on the merits**.

2. *Rejections*

2.1. 35 USC 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 61 and 101 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter; *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims to contain wording such as " An isolated and purified

protein or nucleic acid." It should be noted that recombinant enzymes/proteins are assumed to be identical to those produced naturally unless otherwise indicated.

2. 2. 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 5, 6, 27, 31, 65 and 71 and are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5 and 6 should be corrected to include the word "which" before the word "hybridizes."

Claims 3, 5, 6, 27-29 and 71 are rejected because the phrase "normal stringency conditions" is indefinite. The examiner acknowledges exemplifying normal hybridization conditions on page 9 line, 11 of the application. However, conditions are merely exemplified and there is nothing to suggest that other hybridization are not intended to be included. In the art what conditions are considered "normal" varies widely depending on the situation and person making the determination. Therefore, it is unclear how homologous to a sequence encoding SEQ ID NO:46 a sequence must be to be within the scope of the claim. Specifying the hybridization conditions in the claims will lead to vacating this rejection.

Claim 31 recites the limitation "the probe of claim 17". There is insufficient antecedent basis for this limitation in the claim. Claim 17 is not directed to a probe.

Claim 65 is confusing because it refers to a reference human telomerase, however the claim does not recite the DNA sequence encoding that reference human telomerase. For examination purposes it is assumed that the DNA encoding the reference human telomerase is described by SEQ ID NO:1.

2.3. 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2.3.1. Lack of written description

Claims 1, 2, 4, 11-12, 27-29, 31-32, 61, 65-67, 72-79 and 101 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 2, 4 and 72 are directed to variants of the DNA molecule described by SEQ ID NO:45. Disclosure teaches only one species of the claimed genus, i.e. SEQ ID NO:45, without any identifying characteristics of the other species. The scope of the

claims encompass an extremely large number of DNA molecules having sequences resulting form substitution, deletion and/or insertion of any nucleotide with any other nucleotide and/or any number of any nucleotides. The applicants did not describe how to modify the DNA molecule of SEQ ID NO:45 to obtain the claimed variants. Also, Applicants did not set forth any special functional and structural features of claimed variants. Claims 27-29 and 31-32 are directed to nucleic acid probes that is capable of hybridizing to a nucleic acid molecule encoding a vertebrate telomerase, however the claims are silent of structure of the claimed probes. Moreover, the specification fails to describe the identifying characteristics or properties of such probes except by their function. The claimed genus of the probes is a large variable genus. Although the specification exemplifies several of them the Applicants did not set forth any structural features of said probes.

Claims 5, 6, 11-12 and 61 are directed to DNA molecules that hybridize to a sequence comprising SEQ ID NO:45 or that comprising any of the intronic sequencies or to variants of the DNA molecule that comprises any of intronic sequences. The specification does not contain any disclosure of the function of all DNA sequences that are encompassed by the claims. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. Thus, many functionally unrelated DNAs are encompassed within the scope of these claims.

In the view of the lack of structural and functional characteristics of the variants and probes encompassed by the scope of the claims, Applicants failed to sufficiently

describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize they were in possession of the claimed invention.

2. 3.2. *Scope of enablement*

Claims 1-6, 11-12, 27-29, 31-32, 61, 65-67, 72-79, and 101 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the variant of human telomerase gene described by SEQ ID NO:45, or fragments thereof that will specifically hybridize to SEQ ID NO. 45 under defined conditions, does not reasonably provide enablement for any DNA molecule encoding any human telomerase variant, or any fragment and/or variants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to the extremely large number of DNA molecules that are encompassed by them.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or

absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breath of the claimed invention encompasses any variant of the DNA molecule encoding any human telomerase variant, or the DNA that hybridize to it, or any fragment and/or variants thereof. While methods of gene cloning, mapping, sequencing and manipulating are well known in the relevant art, and skills of the artisans highly developed, identifying all the variants of the human telomerase gene, sequences hybridizing to them under all conditions broadly defined as normal, obtaining all possible fragments and variants of such sequences, as well as variants of the fragments, as determined by the language of the claims is outside the realm of routine experimentation. In addition, the probability of success in obtaining the claimed invention is low.

The example provided by disclosure is the variant of human telomerase gene described by SEQ ID NO:45, which is insufficient to put one of skill in the art in possession of the attributes and features of all variants of the human telomerase, Applicants did not provide any guidance or example how to modify SEQ ID NO:45 to obtain required variants. Without the further guidance on the part of Applicants as to which polynucleotide sequences to choose the experimentation left to those in the art is improperly extensive and undue.

2.4. 35 USC section 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claim 1, 2, 3, 4, 5, 6, 11-12, 27, 28, 29, 31, 32, 34 61, 65-67 and 71-79, are rejected under 35 U.S.C. 102(e) as being anticipated by Cech et al in the US Patent No. 6,093,809 ('809) issued on July 25, 2000, with priority to Oct. 1996.

The claims are directed to an isolated DNA molecule, which:

encodes protein of a vertebrate telomerase,

encodes human telomerase,

comprises any of introns of human telomerase or hybridizes to such DNA,

comprises a sequence encoding a splicing variant of human telomerase,

hybridizes to DNA sequences that are complement to a DNA comprising, DNA encoding human telomerase or its fragments ,

hybridizes to human telomerase but not to its fragment consisting of nucleotides 1624-2012,

is an oligonucleotide of 12-200 nucleotides of human telomerase.

Cech et al disclose the human telomerase gene in SEQ ID NO:224. The sequence is identical to the sequence of human telomerase protein of the instant application (SEQ ID NO:1). The subject matter and the scope of claims 1, 2, 3, 4, 5, 6,

11-12, 27, 28, 29, 31, 32, 34 61, 65-67 and 71-79 is encompassed by the disclosure of '809.

SEQ ID NO: 45 of the instant application which encodes the human telomerase lacking the *α* intron, is comprised by the DNA sequence that encodes the whole human telomerase. Therefore, in the case of claim 71, changing the language from "comprising" to "consisting of" would vacate this rejection.

2. 5. Double patenting

2. 5. 1. Obviousness type provisional double patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1-6,11-12, 27-29, 31, 32, 34, 61, 65-67, 71-79 and 101 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 65-87 of copending Application No. 09/108,401 ('401). Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the respective sets of claims is the same, but scopes are different. Each of the applications is claiming overlapping subject matter including nucleic acids of SEQ ID NO:45, fragments thereof, vectors, and host cells comprising these nucleic acids.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

3. Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

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